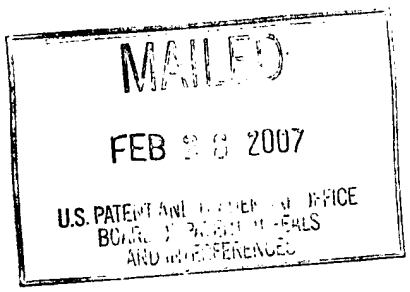
UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte ALEXANDER J. WIGMORE

Appeal 2006-2785
Application 09/831,681
Technology Center 1600



ON BRIEF

Before SCHEINER, MILLS, and GRIMES, *Administrative Patent Judges.*

GRIMES, *Administrative Patent Judge.*

DECISION ON APPEAL

This appeal involves claims to oral drug delivery compositions. The examiner has rejected claims 1-5, 7-9, 16, 30, and 33-36, all of the pending claims, as obvious. We have jurisdiction under 35 U.S.C. § 134.

We reverse the obviousness rejection with respect to claims 1-5, 7, 30, and 34-36.

As to claims 8, 9, 16, and 33, we conclude that the reference cited by the Examiner supports a prima facie case of obviousness, but for different reasons than advanced by the Examiner. We therefore vacate the appealed rejection as to claims 8, 9, 16, and 33, and enter a new ground of rejection.

BACKGROUND

"Allergy to ingested substances can manifest itself in a wide range of symptoms" ranging from gastrointestinal pain to "anaphylactic shock and in some cases death." (Specification 1.) The Specification states that allergy to ingested substances is the likely cause in a portion of patients suffering from chronic diseases "including anaphylactic shock, atopic dermatitis, chronic urticaria, asthma, allergic rhinitis, irritable bowel syndrome, migraine and hyperactivity in children." (*Id.*)

The Specification discloses that the normally inhaled asthma drug, sodium cromoglycate, has been orally administered to treat inflammatory bowel disease and food allergy. (*Id.* at 2.) However, the drug's efficacy "has been reported as being variable with some authorities reporting good effects and others variable or poor effects." (*Id.*)

The Specification states that orally administered sodium cromoglycate powders and gelatin capsules have "low bioavailability because the sodium salt of the drug is converted in the acidic conditions of the stomach into insoluble and inactive cromoglycic acid." (*Id.* at 3.) The Specification states that enteric coated versions of sodium cromoglycate "similarly may be of low bioavailability because the sodium cromoglycate is released from the enteric coating into the duodenum in a lump that does not dissolve, rather than being dispersed evenly throughout the food material passing through the small intestine." (*Id.*)

The Specification discloses orally administered chromone-containing compositions having increased bioavailability. (*Id.* at 4.) The compositions are formulated such that only a small percentage of the drug dissolves after

extended exposure to simulated gastric fluid, but a large percentage of the drug dissolves shortly after subsequent exposure to simulated intestinal fluid. (*Id.*) The compositions may be in the form of tablets or capsules, with enterically coated forms being preferred. (*Id.* at 9.)

DISCUSSION

1. CLAIMS

Claims 1-5, 7-9, 16, 30, and 33-36 are pending and on appeal.

We will focus on claims 1, 8, 9, 16, and 33, which read as follows:

1. An oral drug delivery composition comprising a chromone wherein (1) not more than 10% of the chromone dissolves after two hours exposure of the composition to simulated gastric fluid and (2) at least 15% of the chromone dissolves within 10 minutes of subsequent exposure of the composition to simulated intestinal fluid, said composition further comprising disintegrant at a ratio of at least 1.2:1 (w:w) of disintegrant to chromone wherein said disintegrant is selected from the group consisting of microcrystalline cellulose, croscarmellose sodium, crosprovidone, sodium starch glycolate, and combinations thereof.

8. An oral drug delivery composition comprising a chromone wherein the composition further comprises disintegrant at a ratio of at least 1.5:1 (w:w) of disintegrant to chromone.

9. A composition according to claim 1 or claim 8 wherein the ratio of disintegrant to chromone is between about 1.5:1 and 2.5:1

16. A composition according to any one of claims 1, 8, or 9 wherein the disintegrant is microcrystalline cellulose.

33. A composition according to any one of the preceding claims wherein the chromone is sodium cromoglycate.

Thus, claim 1 is directed to a composition comprising a chromone drug and at least one of several specified disintegrants. Not more than 10%

of the chromone in the composition dissolves when the composition is exposed to simulated gastric fluid for two hours. After the composition has been exposed to the simulated gastric fluid for two hours, and is then exposed to simulated intestinal fluid, at least 15% of the chromone dissolves within 10 minutes.

The specification does not define "simulated gastric fluid" or "simulated intestinal fluid." However, the specification provides examples of those fluids, the simulated gastric fluid having a pH of 1.2, and intestinal fluid having a pH of 5.5 to 7.5. (Specification 10-11.)

Claim 1 also requires the disintegrant and chromone to be in a ratio of at least 1.2:1, on a weight-to-weight basis.

Unlike claim 1, claim 8 does not contain any functional limitation on the dissolution rate of the chromone. Claim 8 recites a composition comprising a disintegrant and chromone drug at a ratio of at least 1.5:1.

Claim 9 limits the disintegrant:chromone ratio in either claim 8 or claim 1 to between about 1.5:1 and 2.5:1. Claim 16 limits the disintegrant in claim 1, 8, or 9, to microcrystalline cellulose. Claim 33 limits the chromone drug in any of the preceding claims to sodium cromoglycate.

2. THE APPEALED REJECTION

Claims 1-5, 7-9, 16, 30, and 33-36 stand rejected under 35 U.S.C. § 103 as being obvious in view of Watts.[1]

The Examiner cites Watts as teaching "a composition for enhanced uptake of polar drugs, including sodium cromoglycate, from the colon."

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[1] Watts et al., U.S. Patent 6,200,602 B1, issued March 13, 2001 (effective U.S. filing date March 30, 1998).

(Answer 3.) The Examiner points out that the composition may comprise microcrystalline cellulose, "and can be formulated into capsule, tablet or pellets." (*Id.*)

The Examiner acknowledges that "Watts does not teach the dissolve rates of the dosage form." (*Id.*) To meet the claimed dissolution rates, the Examiner reasons that, because Watts uses an enteric coating, Watts' composition would have dissolution rates similar to those recited in the claims. (*Id.* at 4.) The Examiner concludes that "[a]ccordingly, it would have been obvious for one of ordinary skill in the art to, by routine experimentation[,] determine a suitable dissolve rate to obtain the claimed invention, because Watts teaches the advantageous results in the use of similar enteric-coated dosage form to ensure the release of drug in the small intestine." (*Id.*)

Appellant argues that Watts does not suggest the claimed dissolution rates. (Br. 18.) Appellant notes that Watts uses an enteric coating that will not dissolve until the composition reaches the colon. (*Id.* at 18-19.) Appellant argues that the dissolution rate of an enteric coating is independent from the dissolution rate of a drug, and that the claims are directed to the dissolution rate of the drug, not the coating. Appellant concludes that the Examiner has failed to make out a prima facie case of obviousness. (*Id.* at 19-20.)

As pointed out by Appellant

> In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. "[The Examiner] can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to

> one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references."

In re Fritch, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (citations omitted, bracketed material in original). Furthermore, "[e]ven when obviousness is based on a single prior art reference, there must be a showing of a suggestion or motivation to modify the teachings of that reference." *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000).

Because the Examiner has not established that one of ordinary skill would have been motivated to produce a composition having the claimed dissolution properties, we agree with Appellant that the Examiner has not established a prima facie case of obviousness with respect to claims 1-5, 7, 30, and 34-36.

Claim 1 is representative of claims 1-5, 7, 30, and 34-36. Claim 1 requires that, after two hours of exposure to simulated gastric fluid, no more than 10% of the chromone in the composition dissolves. Claim 1 also requires that, after the exposure to simulated gastric fluid, within 10 minutes of subsequent exposure to simulated intestinal fluid, at least 15% percent of the chromone dissolves. Thus, the claimed formulations resist degradation in acidic stomach fluid but promptly release the chromone when subsequently exposed to pH-neutral intestinal fluid.

In contrast, Watts' objective is to prepare compositions which pass through both the stomach and small intestine, to release the active ingredient into the colon. (Col. 6, ll. 32-34 ("Any coating can be used which ensures that the capsule, tablet or pellet does not break-up and release the drug until

it is in the colon.").) Thus, Watts' compositions have "[a] thick layer of coating . . . which will dissolve in about 3-4 hours thereby allowing the capsule underneath to breakup only when it has reached the terminal ileum or colon." (Col. 6, ll. 48-51.)

We do not agree with the Examiner that one of ordinary skill preparing Watts' compositions would have obtained the claimed dissolution rates through routine experimentation. In our view, Watts would have led one of ordinary skill to seek to delay drug release for three to four hours, so as to ensure colonic delivery of the drug, rather than seeking prompt drug release upon passage from the stomach to the small intestine. Because Watts' compositions are designed to resist degradation for a significantly longer time than the two hours recited in the appealed claims, one of ordinary skill optimizing Watts' compositions would not have arrived at a composition having the claimed dissolution properties.

The Examiner has not demonstrated that Watts suggests the claimed dissolution rates; therefore, we reverse the obviousness rejection of claims 1-5, 7, 30, and 34-36.

However, claims 8, 9, 16, and 33 do not contain limitations on the composition's rate of dissolution, and therefore stand on a different footing.

Claims 8, 9, 16, and 33 recite compositions having specific ratios of two ingredients: a chromone which may be sodium cromoglycate, and a disintegrant which may be microcrystalline cellulose.

To meet the limitations requiring specific disintegrant to chromone ratios, the Examiner states that, although "Watts is silent as to the amounts [of microcrystalline cellulose] being used . . . , generally, differences in

concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical." (Answer 4.)

Appellant argues that the relative concentrations of disintegrant and chromone are critical, and that Watts does not suggest the claimed disintegrant to chromone ratios. (Br. 17-18; Reply Br. 4-8.)

Appellant's arguments are not without merit. In reviewing the reference, however, we find that it provides disclosures much more relevant than those relied on by the Examiner. We therefore vacate the Examiner's rejection with respect to claims 8, 9, 16, and 33, and enter the following new ground of rejection.

3. NEW GROUND OF REJECTION

Under the provisions of 37 CFR § 41.50(b), we enter the following new ground of rejection: claims 8, 9, 16, and 33 are rejected under 35 U.S.C. § 103(a) as obvious in view of Watts.

Watts discloses compositions for delivering polar drugs to the colon. (Watts, abstract.) Example 8 of Watts provides a composition containing 900 milligrams of microcrystalline cellulose, the disintegrant recited in claim 9, and 325 milligrams of sodium insulin as the active ingredient. (Col. 11, ll. 13-30.)

The weight-to-weight ratio of disintegrant to active ingredient in Example 8 is therefore about 2.77:1, a ratio encompassed by claim 8 ("at least 1.5:1"), and claim 9 ("between *about* 1.5:1 and 2.5:1") (emphasis added). Example 8 of Watts therefore differs from claims 8, 9, 16, and 33 only in that the active ingredient is not sodium cromoglycate.

However, Watts discloses sodium cromoglycate as one of the suitable active ingredients in the colonic delivery compositions. (Col. 5, ll. 33-35.) It would therefore have been obvious to one of ordinary skill in the art at the time the invention was made to substitute sodium cromoglycate for the sodium insulin in the embodiment described in Watts' Example 8, because Watts teaches that sodium cromoglycate is a polar drug suitable for use in the disclosed colonic delivery compositions.

OTHER ISSUES

Claims 5, 16, 30, and 33 appear to be improper multiple dependent claims. Each of claims 5, 16, 30, and 33 depends from another multiple dependent claim, but 37 CFR § 1.75(c) states that "[a] multiple dependent claim shall not serve as a basis for any other multiple dependent claim."

We also note that claim 9 does not end in a period.

SUMMARY

We reverse the obviousness rejection of claims 1-5, 7, 30, and 34-36.

We vacate the obviousness rejection of claims 8, 9, 16, and 33, and enter a new rejection of those claims, based on obviousness. We have considered the arguments in the Appeal Brief and Reply Brief, but do not find them persuasive with respect to the new ground of rejection.

TIME PERIOD FOR RESPONSE

This decision contains a new ground of rejection pursuant to 37 CFR § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 CFR § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review.

37 CFR § 41.50(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

> (1) *Reopen prosecution.* Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner . . . .
>
> (2) *Request rehearing.* Request that the proceeding be reheard under § 41.52 by the Board upon the same record . . . .

REVERSED-IN-PART, 37 CFR § 41.50(b)

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